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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,568	05/15/2001	Samuel Bogoch	9425/46702	8438

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KENYON & KENYON
Suite 700
1500 K Street, N.W.
Washington, DC 20005

EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	PAPER NUMBER
1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/854,568	BOGOCH, SAMUEL	
	Examiner	Art Unit	
	Stephen L. Rawlings	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed July 15, 2008, is acknowledged and has been entered in part. Claims 1 and 14 have been amended.

2. Claims 1-4 and 14 are pending in the application and currently under prosecution.

Response to Amendment

3. The amendment filed on November 15, 2006, is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). However, in order to advance prosecution, rather than mailing a Notice of Non-Compliant Amendment[1], Applicant is advised to correct the following deficiency in replying to this Office action:

The amendment is non-compliant because it apparently directs the replacement of two paragraphs by reference to the page and line number of the corresponding paragraphs, as found in the originally filed specification, rather than by directing those paragraphs appearing in the substitute specification filed August 15, 2005.

Amendments to the specification that replace paragraphs must be made by submitting an instruction, which unambiguously identifies the location of the paragraphs of the immediate prior version of the specification to be replaced.

Only the corrected section of the non-compliant amendment must be resubmitted (in its entirety), e.g., the entire "Amendments to the specification" section of applicant's amendment must be re-submitted. 37 CFR § 1.121(h).

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[1] See M.P.E.P. § 714.03.

Priority

4. Applicant's claim under 35 U.S.C. §§ 119(e) and/or 120, 121, or 365(c) for benefit of the earlier filing date of Application No. 08/031,562, filed March 16, 1993, which is a continuation-in-part of Application No. 07/744,649, filed August 8, 1991, which is a continuation of Application No. 07/227,621, filed August 3, 1988, which is a continuation of Application No. 06/281,883, filed July 9, 1981, which is a continuation-in-part of Application No. 05/922,799, filed July 7, 1978, and a continuation-in-part of Application No. 06/019,078, filed Mar. 9, 1979, which is a continuation-in-part of Application No. 05/941,940, filed September 13, 1978, which is a continuation of Application No. 05/852,200, filed Nov. 17, 1977, which is a continuation of Application No. 04/621,112, filed October 9, 1975, which is a continuation-in-part of each of Application No. 04/553,075, filed February 25, 1975, Application No. 04/550,432, filed Feb. 18, 1975, Application No. 04/450,404, filed Mar. 12, 1974, and Application Ser. No. 04/385,451, filed Aug. 3, 1973, is acknowledged.

However, claims 1-4 and 14 do not properly benefit under § 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). See M.P.E.P. § 201.11.

In addition, as previously noted, claim 14 does not properly benefit under §§ 119 and/or 120 by the earlier filing dates of any prior applications filed before Application No. 06/019,078, filed March 9, 1979, because none of those application describe "Recognin-M", the process by which that substance is made or isolated, or any process by which it is used.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely May 15, 2001.

Notably, beginning at page 6 of the amendment filed July 15, 2008, Applicant has remarked that the claims are entitled to the filing date of Application No. 07/744,649, filed August 8, 1991, because the Examiner has acknowledged that this application provides written support for the language of the claims and an enabling disclosure of the claimed invention.

In response, contrary to Applicant's assertion, the Office has made no such acknowledgement; if the present application fails to provide adequate written description and a sufficiently enabling disclosure to satisfy the requirements set forth under § 112, first paragraph, so must the earlier filed applications to which this application claims priority. So, for the reasons set forth in the preceding paragraphs, the effectively filing date of claim 1-4 and 14 is deemed the filing date of the instant application, namely May 15, 2001.

Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, Applicant's amendment and/or arguments have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed March 17, 2008.

Grounds of Objection Maintained

Specification

6. The objection to the specification because the use of improperly demarcated trademarks is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears that Applicant has made a *bona fide* attempt to remedy this deficiency by appropriately amending the specification, the amendment to the specification filed July 15, 2008, is not compliant and has not been entered.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

New Grounds of Objection

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Claims 1 and 14, as presently amended, recites limitations describing the polypeptides to which the claims are directed.

M.P.E.P. § 608.01(o) states:

> While an applicant is not limited to the nomenclature used in the application as filed, he or she should make appropriate amendment of the specification whenever this nomenclature is departed from by amendment of the claims so as to have clear support or antecedent basis in the specification for the new terms appearing in the claims. This is necessary in order to insure certainty in construing the claims in the light of the specification, *Ex parte Kotler,* 1901 C.D. 62, 95 O.G. 2684 (Comm'r Pat. 1901). See 37 CFR 1.75, MPEP § 608.01(i) and § 1302.01.

M.P.E.P. § 608.01(o) further states that if the examiner determines that the claims presented late in prosecution do not comply with 37 CFR 1.75(d)(1), applicant will be required to make appropriate amendment to the description to provide clear support or antecedent basis for the terms appearing in the claims, provided no new matter is introduced.

Although it appears that written support for at least some elements of the limitations describing the polypeptides "malignin" and "Recognin-M" to which the claims

are directed may be found in Application No. 07/744,609, which has been incorporated by reference in this application, it is submitted that it would not be clear from a reading of the descriptive portion of this application, alone, where there is support for the language of the claims[2].

Accordingly, Applicant should incorporate the relevant disclosures set forth in Application No. 07/744,609, which are necessary to provide antecedent basis in the instant application for the language of the claims.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The rejection of claims 1-4 and 14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Beginning at page 7 of the amendment filed July 15, 2008, Applicant has traversed the propriety of maintaining this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

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[2] Notably, too, M.P.E.P. § 608.01(p) does not provide for the incorporation by reference of essential material by reference to non-patent publications, such as Application No. 07/744,649. "Essential material" is defined as "that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)". The description of the polypeptides "malignin" and "Recognin-M", which has been added to the claims by the amendment filed July 15, 2008, is considered essential material.

In this instance, the claims are directed to substances termed “malignin” and “Recognin-M”, which are to be administered to a subject in an amount effective to stimulate an immune response in the subject, and more particularly to elicit the production of an antibody that binds to these substances, so as to inhibit the growth or proliferation of glioma cells expressing “malignin” or kill breast cancer cells expressing “Recognin-M” in the subject.

As previously explained, the precise, detailed structures of the substances termed “malignin” and “Recognin-M” are not known or disclosed, but may have varying structures (e.g., different molecular weights).

Nonetheless, according to the disclosure at page 17 of the specification, as originally filed, the polypeptides identified as “malignin” and “Recognin-M", which are described by Application No. 07/744,649 (now abandoned), may be used to prepare the compositions to which the claims are directed.

Application No. 07/744,649 describes the isolation of a “malignin” polypeptide from glioma tumor tissue, which has a molecular weight of about 10 kDa and an amino acid composition identical to that which is presently recited in claim 1; see pages 31 and 32 of the specification, as originally filed in that application.

However, in contrast to the polypeptide described by Application No. 07/744,649, the polypeptide to which claim 1 is directed need not be isolated from glioma cells; accordingly, claims 1-4 are more broadly directed to any of a genus of polypeptides having the structural and physical properties, which are now recited in claim 1.

In addition, Application No. 07/744,649 describes the isolation of a “Recognin-M” polypeptide from MCF7 breast cancer cells, which has a molecular weight of about 8 kDa and an amino acid composition identical to that which is presently recited in claim 1; see pages 34-36 and Table III at page 38 of the specification, as originally filed in that application.

However, again in contrast to the polypeptide described by Application No. 07/744,649, the polypeptide to which claim 14 is directed need not be isolated from MCF7 cells; accordingly, claim 14 is more broadly directed to any of a genus of

polypeptides having the structural and physical properties, which are now recited in claim 14.

As explained in the preceding Office action, the specification discloses that the vaccine (i.e., the composition comprised of the substances termed “malignin” or “Recognin-M”) can be entirely produced from tissues or cells, or it may be entirely synthetic (paragraph [0034] of the published application); yet, the specification does not describe the materials that are the substances to which the claims are directed, but only a method for isolating those substances.

The polypeptides to which the claims are directed cannot be made "synthetically", as might be done *in vitro* or in cell culture using recombinant DNA technology, or using a peptide synthesizer. Since the structures of the polypeptides are unknown (e.g., the amino acid sequences of the polypeptide backbones of these polypeptides are unknown), it would not be possible to use a machine to synthesize the proteins and a nucleic acid molecule encoding a polypeptide having the primary structures of “malignin” and “Recognin-M” cannot be produced or used in the synthesis.

As further explained in the preceding Office action, since the specification describes the substances termed “malignin” and “Recognin-M” as glycoproteins (i.e., conjugated proteins having a carbohydrate component), or derivatives thereof, having a molecular mass of about 10 kDa (see, e.g., paragraph [0013] of the published application), it is aptly noted that the antigenic determinants of which the substances are comprised, which elicit antibodies capable of inhibiting the growth of the cancer cells, may not be contained by the peptide backbone. Instead it is just as probable that the immunogenicity of the substances is an attribute of the carbohydrate moieties or the junctions of these moieties and the peptide. If that is the case, synthesizing a peptide having the amino acid sequence of the substances termed “malignin” and “Recognin-M” would not necessarily produce an immunogen capable of eliciting the requisite immune response in the subject, which is directed against the cancer cells.

Therefore, the specification would at best provide an adequate written description of the products produced by processes that are clearly and particularly described in this application (and isolated from the same sources described in Application No.

07/744,649), as opposed to any product that might be deemed immunologically the same or equivalent to those products that were isolated and purified by those processes.

Again, Applicant is reminded that "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

In this instance, the language that describes the polypeptides termed "malignin" and "Recognin-M" fail to point out the particular polypeptides, which can be used in practicing the claimed process to achieve the claimed therapeutic effect, since the polypeptides need not be isolated from the same sources by the same processes described.

Moreover, Applicant is again reminded that the Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Because the specific nature and substance of "malignin" and "Recognin-M", which gives rise to the desired immune response in the subject is unknown, there is in fact such unpredictability.

For example, even if a 10 kDa protein resembling "malignin" in amino acid composition were known, it could not be predicted whether that protein is capable of eliciting an anti-glioma immune response of sufficient magnitude and/or specificity to inhibit the growth of those cancer cells, especially if the protein used to formulate the composition to which the claims are directed is not the same protein that is expressed by the cells.

If the polypeptides need not be isolated from the cells from which the polypeptides were first isolated, even polypeptides having identical molecular weights and amino acid compositions may not elicit immune responses against those cells expressing the polypeptides first isolated.

Importantly, as noted in the preceding Office action, it is not the amino acid composition of an antigenic protein that gives rise to a specific immune response against that protein; rather it is the protein's three-dimensional structure, determined in part by its amino acid sequence and the conformation assumed by the molecule in space.

Then, since the protein is apparently derived from a glycoprotein precursor, it is just as likely that the specific immune response elicited by the protein, which is effective to inhibit the growth of cancer cells, is attributable to the structure of the carbohydrate moieties of which it is comprised.

There is simply no way of meaningfully predicting whether any 10 kDa glycoprotein having an amino acid composition resembling "malignin" might be capable of eliciting the requisite immune response in the subject.

While the written description requirement can by satisfied without an actual reduction to practice, the disclosure of the processes by which products termed “malignin” and “Recognin-M” were isolated and purified by Applicant is not sufficient to satisfy that requirement, unless the products to which the claims are directed are necessarily products produced by those processes, since otherwise there is simply no way of knowing whether either one of the products is at hand.

Furthermore, merely having disclosed the recognized functional attribute of the substances isolated and purified by the disclosed processes, rather a recitation of their precise structures does not satisfy the written description requirement.

The claimed method depends upon knowing those polypeptides to which the claims are directed, namely those polypeptides termed “malignin” and “Recognin-M”, which can be used to achieve therapeutic effect in treating glioma or breast cancer in subjects in accordance with the claims; without such substances, it is impossible to practice the invention.

Although the skilled artisan could potentially identify substances, perhaps having the same molecular weight or the same amino acid composition as the product isolated and purified by processes disclosed in this application, albeit from different sources of cells or tissues, which might be used in practicing the claimed inventions to achieve the

claimed effects, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

For all of the above reasons, it is submitted that the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed, so as to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

10. The rejection of claims 1-4 and 14 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a process for inhibiting the growth or proliferation of glioma cells in a subject, said process comprising administering to said subject a composition comprising an amount of malignin effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-malignin antibody, which is binds to and inhibits glioma cells in the subject, wherein said malignin is that substance that is produced by the process described in Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 11 of this application, **and for using** a process for killing breast cancer cells in a subject, said process comprising administering to said subject a composition comprising an amount of Recognin-M effective to stimulate the immune system of the subject, so as to cause the production

and release of an anti-Recognin-M antibody, which is binds to and inhibits glioma cells in the subject, wherein said Recognin-M is that substance that is produced by the process described in Examples 5B, beginning at page 34 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 36 of Application No. 07/744,649, **does not reasonably provide enablement for using** the claimed process, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Beginning at page 7 of the amendment filed July 15, 2008, Applicant has traversed the propriety of maintaining this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

As explained in the above rejection of the claims, as failing to satisfy the written description requirement, the specification, as filed, is only sufficient enabling of the isolation and purification of the substance termed "malignin", which is produced by the process described in Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 11 of this application.

This process, which is described in the earlier filed application, expressly comprises isolating the claimed "malignin" polypeptide from glioma tumor tissue.

There is no evidence reasonably suggesting that the polypeptide that might be used to practice the claimed process, so as to achieve the claimed objective, could be isolated from any different source; yet the claims are not limited to a polypeptide that is necessarily isolated from glioma cells.

The specification, as filed, would not reasonably enable the skilled artisan to make or synthesize by any other means the substance termed "malignin" to which the claims are directed, which substance is effective to elicit in a subject an immune response that leads to the production of anti-malignin antibodies that bind to and inhibit the growth and/or proliferation of glioma cells in the subject without undue and/or unreasonable experimentation since the immunogenic and therapeutic properties of any other substance, or the specificity and/or therapeutic effects of antibodies produced in response to immunization thereby, cannot be known or predicted.

In addition, as also explained in the above rejection of the claims, as failing to satisfy the written description requirement, the specification, as filed, is only sufficient enabling of the isolation and purification of the substance termed “Recognin-M”, which is produced by the process described in Examples 5B, beginning at page 34 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 36 of Application No. 07/744,649.

This process, which is described in the earlier filed application, expressly comprises isolating the claimed “Recognin-M” polypeptide from MCF7 cells.

There is no evidence reasonably suggesting that the polypeptide that might be used to practice the claimed process, so as to achieve the claimed objective, could be isolated from any different source; yet the claims are not limited to a polypeptide that is necessarily isolated from glioma cells.

Then, as further explained in the preceding Office action, the specification, as filed, would not reasonably enable the skilled artisan to make or synthesize by any other means the “malignin” or "Recognin-M" polypeptides to which the claims are directed, and which are effective to elicit in a subject an immune response that leads to the production of anti-malignin or anti-Recognin-M antibodies that bind to and kill glioma or breast cancer cells in the subject without undue and/or unreasonable experimentation. Again, this is because the immunogenic and therapeutic properties of any other substance, or the specificity and/or therapeutic effects of antibodies produced in response to immunization thereby, cannot be known or predicted.

Finally, though the "malignin" and "Recognin-M" polypeptides to which the claims are directed have some of the structural and physical characteristics of the polypeptides that were isolated from glioma and MCF-7 breast cancer cells, the polypeptides are not necessarily isolated by the same steps that led to the isolation of the polypeptides described, which allegedly may be used as immunogens to elicit antitumor immune responses in subjects suffering from glioma or breast cancer. If the isolation protocols by which the polypeptides are isolated are varied, it is reasonable to expect variations in the products that are yielded upon completion of those protocols, particularly in this instance where it seems the polypeptides may have varying molecular weights and perhaps differing amino acid compositions, and it is unclear which one or more of the polypeptides that was first isolated may have the immunological properties that account for their ability to stimulate the antitumor immune response in the subjects.

Accordingly, it is again submitted that at best the specification is only reasonably enabling of the use of a process for inhibiting the growth or proliferation of glioma cells in a subject, said process comprising administering to said subject a composition comprising an amount of malignin effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-malignin antibody, which is binds to and inhibits glioma cells in the subject, *wherein said malignin is that substance that* is *produced by the process described in Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649*, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 11 of this application, and reasonably enabling of the use of a process for killing breast cancer cells in a subject, said process comprising administering to said subject a composition comprising an amount of Recognin-M effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-Recognin-M antibody, which is binds to and inhibits glioma cells in the subject, *wherein said Recognin-M is that substance that is produced by the process described in Examples 5B, beginning at page 34 of the specification of Application No. 07/744,649*, which substance is characterized as having a molecular weight of approximately 10,000

Daltons and the amino acid composition set forth at page 36 of Application No. 07/744,649.

In conclusion, although Applicant's arguments have been carefully considered, upon equally careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), it has been determined that the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would have been insufficient to have enabled the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. The rejection of claims 1-4 under 35 U.S.C. 103(a), as being unpatentable over Bogoch et al. (1984) (of record; cited by Applicant as Reference #6) and Bogoch et al. (*Prog. Clin. Biol. Res.* 1980; **39**: 407-424) (of record; cited by Applicant), is maintained.

Beginning at page 8 of the amendment filed July 15, 2008, Applicant has traversed the propriety of maintaining this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Bogoch et al. (1980) teaches the survival rate of cancer patients with low level of serum anti-malignin antibody is poorer, as compared to cancer patients with relatively high level of serum anti-malignin antibody; see entire document (e.g., page 422). Bogoch et al. teaches the antibody thus seems to be beneficial (page 422). Moreover, Bogoch et al. teaches anti-malignin antibody is cytototoxic to malignant glial cells *in vitro* (page 422). Finally, Bogoch et al. teaches the antibody preferentially binds to glioma cells *in vivo* (page 422).

Bogoch et al. (1984) suggests that anti-malignin antibody has therapeutic properties; see entire document (e.g., page 746). Bogoch et al. further suggests that stimulating the production of anti-malignin antibody, so as to replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient, by active or passive immunotherapy will be clinically effective against cancer (page 746).

In view of the teachings of Bogoch et al. (1980) and Bogoch et al. (1984), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have administered to a subject an amount of a composition comprising malignin, which is effective to stimulate the immune system of the subject, so as to produce and release anti-malignin antibody into the subject's serum, because Bogoch et al. (1980) suggests that doing so to stimulate the production of anti-malignin antibody, and to thereby replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient, will be clinically effective against cancer. One of ordinary skill in the art at the time the invention was made would have been motivated to have done so in order to treat a

glioma in the subject. One of ordinary skill in the art at the time the invention would have had a reasonable expectation of successfully treating glioma by doing so because Bogoch et al. (1984) teaches the survival rate of cancer patients with low level of serum anti-malignin antibody is poorer, as compared to cancer patients with relatively high level of serum anti-malignin antibody, the antibody preferentially binds to glioma cells *in vivo*, and it is cytototoxic to glioma cells.

Applicant has argued that "[there] is no expectation of success in a simple suggestion" (page 9, paragraph 2).

In response, there need not be an expectation of success associated with the suggestion, per se; the concepts are different elements of the factual inquiry that is made in determining the obviousness of the claimed invention.

In further response, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as noted in the paragraphs above, Bogoch et al. (1980) suggests administering to a subject suffering from a glioma an amount of a composition comprising malignin, which is effective to stimulate the immune system of the subject, so as to elicit the production and release of anti-malignin antibody into the subject's serum, and to thereby replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient. Bogoch et al. (1984) expressly suggest that doing so will be clinically effective against cancer.

Then, as also explained, it is submitted that one of ordinary skill in the art at the time the invention would have had a reasonable expectation of successfully treating glioma by doing so because Bogoch et al. (1984) teaches the survival rate of cancer patients with low level of serum anti-malignin antibody is poorer, as compared to cancer patients with relatively high level of serum anti-malignin antibody, the antibody preferentially binds to glioma cells *in vivo*, and it is cytototoxic to glioma cells.

Citing the Office action mailed August 15, 2005, Applicant has argued that the Office previously acknowledged that a correlation between survival and serum anti-malignin antibody concentration is insufficient to provide the artisan with an expectation of success.

In response, there is no Office action mailed August 15, 2005; but if Applicant intended to refer to the Office action mailed February 15, 2005, it does not appear that that Office action acknowledges that a correlation between survival and serum anti-malignin antibody concentration is insufficient to provide the artisan with an expectation of success. Rather that Office action, at page 11, appears to discuss a lack of correlation between results of experiments performed *in vitro* and results of experiments performed *in vivo*. It does not however appear to address the significance of a correlation between the survival and serum levels of an anti-malignin antibody, which according to Bogoch et al. (1984) exists.

At page 9, paragraph 3, Applicant has remarked that the specification does not suggest that the correlation of survival and high serum levels of anti-malignin antibody in patients provides the artisan with a reasonable expectation of success.

In reply, it is irrelevant whether the specification makes such a suggestion since the question of the obviousness of the claimed invention is not properly based in the teachings of the specification, but rather the teachings and suggestions found either in the prior art or in the knowledge generally available to one of ordinary skill in the art.

At page 10, paragraph 1, Applicant has further argued that the artisan would not have had a reasonable expectation of success because any reasonable expectation of success would be based on a range of confirmatory data.

In response, it might be argued that the prior art is as enabling as the specification, since neither discloses “confirmatory data” that proves the claimed process may be used to achieve the claimed effect[3], but nonetheless it is submitted that

[3] Notably, the use of the claimed invention to achieve clinically significant inhibition of the growth and proliferation of glioma cells in a subject has not been demonstrated in this application; and it appears that much of the exemplary disclosure addresses the functional properties of an "anti-Recognin antibody", as opposed to an anti-malignin antibody, where it appears that “Recognin” and “malignin” are not the same polypeptides.

the prior art suggests that administering to a subject suffering from a glioma an amount of a composition comprising malignin, which is effective to stimulate the immune system of the subject, so as to elicit the production and release of anti-malignin antibody into the subject's serum, and to thereby replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient will be clinically effective against cancer.

In further response, it is aptly noted that in citing Bogoch et al. (1984), Bogoch et al. (1988) teaches "[human] antimalignin antibody (AMA) appears to have clinical significance because in actuarial studies its concentration relates quantitatively to survival (Bogoch et al. Protides Biol Fluids 1984; 31:739-747)" (abstract). Thus, it is submitted that the artisan of ordinary skill in the art, guided by such disclosures, would have concluded that stimulating the immune system of the subject by administering to the subject an immunogenic composition comprising malignin, so as to elicit the production and release of anti-malignin antibody into the subject's serum, is reasonably expected to have clinically significant therapeutic effect.

Finally at page 10 of the amendment filed July 15, 2008, citing the Office action mailed February 15, 2005, Applicant has argued that the Office previously argued that an expectation of success cannot be based simply on the correlation data provided in the application.

Notably, the Office's arguments that are referred to are those that are set forth in the rejection of the claims under 35 U.S.C. §112, first paragraph, as failing to provide an enabling disclosure of the claimed processes. That ground of rejection has been withdrawn.

In further response to this last argument, Applicant is directed to consider their arguments set forth at pages 9 and 10 of the amendment filed August 15, 2005, in traversing the enablement rejection, which reads, with emphasis added:

> The claims, as amended, are not directed to "a cure for cancer" **and do no purport to alone protect against or treat cancer**. Instead, they are directed to assisting the body in conjunction with other therapies by administering malignins to "stimulate the immune system." **The fact that the stimulation of the immune system causes**

> **production of anti-malignin antibodies indicates that stimulation of the immune system has indeed occurred**.
>
> Although not wishing to be bound by theory, the specification suggests "anti-Recognin is a general inhibitory transformation antibody whose augmentation may be useful in efforts at the immune prevention and treatment of cancer." Appln. at ¶ [0012]. **The skilled artisan would understand that the plural "efforts" of paragraph 12 are not restricted to the presence of anti- malignin antibody alone but to its presence in conjunction with other efforts**.
>
> Furthermore, the specification teaches that the anti-malignin antibody is present in healthy individuals and rises with increase in cancer risk and presence of cancer, see Appln. at ¶ [0005], and that increases in concentration of the anti-malignin antibody are correlated with survival in cancer patients. See Appln. at ¶ [0009]. **The artisan would understand from these data and the instructions of the specification that "[t]he present invention describes products[, namely malignins,] to aid both cancer prevention and cancer treatment**." Appln. at ¶ [0008].
>
> Moreover, **it was known in the art at the time of filing that products that aid the immune response can be very important in assisting the total immune response to an antigen of interest. The artisan would have understood, on review of the application, that augmentation of the immune response to an antigen is sometimes as important as presenting the antigen itself to the immune system**.
>
> The specification fully describes to one of skill in the art how to stimulate the immune system with malignin to assist in cancer treatment or conventional cancer therapy. As such, the claims are enabled. Accordingly, Applicant respectfully requests withdrawal of the present rejection of the claims for lack of enablement.

Again, the rejection has been withdrawn in favor of Applicant's arguments that the artisan would have had a reasonable expectation of success of using the claimed process to achieve the claimed objective.

This is in part because, as Applicant has remarked, "the specification teaches that the anti-malignin antibody is present in healthy individuals and rises with increase in cancer risk and presence of cancer, [...] and that increases in concentration of the anti-malignin antibody are correlated with survival in cancer patients [, such that the] artisan would understand from these data and the instructions of the specification that '[t]he present invention describes products[, namely malignins,] to aid both cancer prevention and cancer treatment' " (paragraph bridging pages 9 and 10 of the amendment filed August 15, 2005).

Accordingly, since the prior art in fact teaches that which Applicant has remarked the specification teaches, namely that increases in concentration of the anti-malignin antibody are correlated with survival in cancer patients, and since *Applicant* has argued that given such teaching the artisan would understand that stimulating the immune system of the subject by administering to the subject an immunogenic composition

comprising malignin, so as to elicit the production and release of anti-malignin antibody into the subject's serum, will have clinically significant therapeutic effect, the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the prior art's teachings and moreover the artisan would have had a reasonable expectation of success in using the invention to achieve therapeutic effect in the subject suffering from glioma.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-4 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 and 14 are indefinite for the following reason:

Claims 1 and 14 contain the trademark/trade name Sephadex™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a resin used for chromatography and, accordingly, the identification/description is indefinite.

16. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a “new matter” rejection.

Claim 14 is directed to a “Recognin-M” polypeptide having a molecular weight of "approximately 10,000 Daltons", which “elutes, in a 0.5 M phosphate buffer, pH 7.2, at a discrete spot of approximately 0.9 with reference to a standard of cytochrome C when chromatographed on a Sephadex G-50 resin column".

Applicant has remarked at page 6 of the amendment filed July 15, 2008, that support for the language of the claim, as presently amended, is found, for example, in Example 5B beginning at page 34 of Application No. 07/744,649.

Contrary to Applicant’s assertion it does not appear that Application 07/744,649 describes a “Recognin-M” polypeptide having a molecular weight of "approximately 10,000 Daltons", which “elutes, in a 0.5 M phosphate buffer, pH 7.2, at a discrete spot of approximately 0.9 with reference to a standard of cytochrome C when chromatographed on a Sephadex G-50 resin column".

According to Table III at page 48 the isolated "Recognin-M" polypeptide had a molecular weight of 8,000 Daltons; and not inconsistently, the application also discloses at page 41, lines 13-15, that “[thin] layer chromatography with Sephadex G200 (Pharmacia) gave a molecular weight for both Recognin L and Recognin M of approximately 8,000, the same as that obtained with Astrocytin.”

As for whether or not the isolated polypeptide “elutes, in a 0.5 M phosphate buffer, pH 7.2, at a discrete spot of approximately 0.9 with reference to a standard of cytochrome C when chromatographed on a Sephadex G-50 resin column", no disclosure describing the polypeptide could be found in Application No. 07/744,649.

For these reasons it appears that the amendment to claim 14 has introduced new matter into the specification of this application, thereby violating the written description requirement set forth under 35 U.S.C. § 112, first parargraph.

This issue might be remedied if Applicant were to point to particular disclosures in this application or in Application 07/744,649 (which has been incorporated by reference), which are believed to provide the necessary written support for the language of the claim.

Conclusion

17. No claim is allowed.

18. Applicant is advised that it appears that any patent that issues from this application, were this application deemed to benefit from the filing date(s) of the prior filed applications, as presently sought by Applicant, would be unenforceable, as the patent term will have expired immediately following its issue. The expiration date of the patent term will be determined from the earliest effective U.S. filing date of this application.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

slr
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